

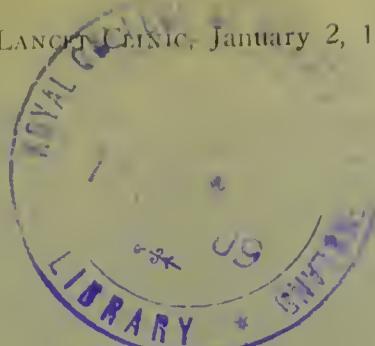
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HYPERTHYROIDISM AND BASEDOW'S DISEASE.

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Reprinted from THE LANCET-CLINIC, January 2, 1909.





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IN 1786 Parry, who, according to Möbius, is really entitled to the credit of first writing upon this disease, described it as an enlargement of the thyroid gland with palpitation, cardiac hypertrophy, exophthalmos, and a disturbance of the nervous system.

In 1835, or about a half century after Parry, Graves described it as related to hysteria. The English gave it the name of Graves' disease; but not until 1840, or more than half a century after Parry, did von Basedow's writings make their appearance. It is only, however, in recent years that it has attracted unusual attention. This is due largely to our better knowledge of the disease, whereby we are able to recognize it not only in its earlier stages, but also in its more atypical forms. Where the clinical triad of vascular struma, exophthalmos and tachycardia with vascular changes are well marked, its recognition is unmistakable. There is a large class of atypical cases, such as *formes frustes* of Troussseau, where the diagnosis is not so easy, at least without some time for study and observation.

These cases have frequently drifted from the internist to the neurologist or the ophthalmologist, until, through the lapse of time and the more perfect development of symptoms, their real nature becomes apparent.

In addition to the three cardinal symptoms already noted, may be mentioned tremor, restlessness, insomnia, psychic disturbances, muscular weakness, diarrhea and the loss of weight. In the skin we have excessive pigmentation, deficient pigmentation, erythema, urticaria, perspiration, edema, and the loss of hair. In addition to the acceleration of the heart, we have also dilatation of the right side, and later degeneration. Not only is the symptom-complex extensive in its scope, but almost every symptom is capable of equally

extensive variation in each individual case, which goes far towards explaining the diagnostic difficulties in atypical and early cases. Many are misled through the apparent lack of enlargement of the struma. A sufficiently clear distinction is not always made between changes in the thyroid gland and an enlargement of the thyroid gland. The changes in the gland may not be attended by any apparent enlargement, and may only be appreciated by a microscopic section. By microscopic section, however, it is plain that we have changes that consist of an increased number of cells and conditions pointing to an increasing activity of such cells without necessarily giving rise to more than a slight enlargement of the gland after it is exposed in an operative way.

On the other hand, a considerably enlarged gland may be an underactive gland in that the type may be fetal in character, or the enlargement may be due to a colloid condition, which is always a condition of inactivity because of its degenerated character.

Notwithstanding the attention it has received in recent years, there is yet much work ahead before its causation and pathology are entirely settled.

The most generally accepted view is that of Möbius, that it is a trophoneurosis due to a toxin dependent either upon an excessive amount of normal or abnormal secretion, or perhaps both. Many believe that the disease cannot be produced in its entirety by the administration of thyroid tablets, and therefore contend that an excessive amount of the normal secretion alone is incapable of producing the disturbance. It is plain, however, that whatever the toxin is, it is elective in its action, exerting its influence principally upon the heart, blood-vessels, central nervous system and skin.

According to Möbius, the disease may

* Read before the Tenth Annual Meeting of the Ohio Valley Medical Association, French Lick, Ind., November 11-12, 1908.

be primary or secondary, *i.e.*, the symptoms may precede a struma or they may be engrafted upon a struma secondarily. Klenim and others think it is always primary.

It may be acute, terminating in death in a few months, but more frequently is chronic in character, lasting many years. There may be periods of remission, in which there is such an improvement as to make them think themselves well.

In an analysis of 980 cases by Buschan, 805 were in women and 175 in men, or 4.6 to one. Murray and McKenzie found the relation to be 1 to 10. It most frequently occurs between the years of sixteen and forty. According to von Graefe and Möbius, it is usually severer in men than in women.

In a series of 106 cases examined under Kocher's direction, the red corpuscles were normal in number, while the white were diminished from 7,000 to 5,000, and in one case to as low as 3,700. Kocher believes that in the careful examination of the blood we will be able to make the earliest and most trustworthy diagnosis and prognosis. He believes that in animals, as in different races, histological differences occur in the thyroid gland which predispose some to the occurrence of Basedow's disease. This Basedow constitution is what we would call a sanguineous temperament, *i.e.*, the opposite to the phlegmatic temperament—the types that are restless, reactive, and show, through blushing, perspiration and tremor, the result of an impression. In Basedow's disease the blood does not coagulate as readily as in the normal, hence a tendency to bleeding. He found a reduction of polynuclear neutrophile leucocytes from 5,000 to 1,537, or from 75 per cent., the normal amount, to 35 per cent. This, together with the increase of lymphocytes, the latter increasing from 1,500 to 2,000, the normal amount to 5,875, or from 25 per cent. to 57 per cent., represent the most characteristic features of the blood in Basedow's disease.

In individual cases on the day of operation or the next, he found the neutrophiles increased from 42 per cent. to 89.2 per cent., whereas the lymphocytes decreased from 48 per cent. to 2.7 per cent. In another case, two days after the operation, the leucocytes increased from 6,500 to 9,000. The neutrophiles increased from 63 per cent. to 84 per cent., and the lymphocytes fell from 28.6 per cent. to 10 per

cent. The eosinophiles disappeared entirely. In other words, he concludes that we have in Basedow's disease an increasing lymphocytosis and a decreasing leucocytosis before the operation, and after the operation the reverse. In acute infectious troubles there occurs a neutrophile leucocytosis. The neutrophile contains antitoxic, peptic, oxidative ferments, and possesses intense chemotactic properties. For that reason their reduction makes the Basedow subject a poor one for any operation. According to Kocher, the specific character of the morbus Basedowii is a hyperthyreosis with glandular hyperplasia, lymphocytosis and lymphatic disturbances of the gland. This explains the relationship of Basedow's disease to Mikulicz's disease, lymphatic leukemia and pseudo-leukemia.

The medical treatment, although of value in preparing a certain class of cases for operative attack, hardly in itself offers enough to suggest it as a substitute for surgical interference. We might, therefore, say that there are two courses open, the serum and surgical interference. The serum in the hands of a few seems to have yielded some results. It is not easy to obtain, and its exact position remains to be determined.

According to Rogers (*Annals of Surgery*, Vol. 47, p. 790), "the antithyroid serum is made by injecting rabbits or sheep with the combined nucleo-proteid and thyro-globuline obtained from the human thyroid gland. The serum made from the pathological gland of Graves' disease has probably a better therapeutic effect than that made from the normal organ. Certain patients, however, do not improve under the administration of antiserum, or rather under antithyroid treatment, and prothyroid treatment must be employed, either alone or in combination with the antiserum. For this purpose there can be given by mouth the nucleo-proteid material of sheep thyroids, or by hypodermic the nucleo-proteid material derived from the normal human thyroid."

The surgical treatment seems destined to be the finally accepted method of cure, and when employed should be undertaken early enough to avoid the permanent changes that attend some of the late cases and prevent complete restoration of the normal status.

According to Crile (*Annals of Surgery*, Vol. 47, page 864), "we may accept as proven the fundamental proposition that if

a sufficient amount of the thyroid gland in Graves' disease be successfully excised, relief or cure will follow. Whether the relief or cure be complete or incomplete, is dependent upon the correct or incorrect judgment in estimating the amount of gland tissues to be removed."

Hartley (*Annals of Surgery*, Vol. 42, p. 33) lays down the following axioms:

1. That "the whole story of Basedow's disease lies in the thyroid gland" (Kümmell).

2. That "chemically it makes no difference whether the secretion of the gland is increased or is chemically altered as the result of the changes in the blood, in the alimentary canal, or in the central nervous system; the fact remains that the removal of the growing gland does away with the symptoms, and upon the failure to remove the diseased glands depends the failures to cure" (Schulz).

3. That "the characteristic pathological change in the gland is a diffuse parenchymatous hypertrophy. Where goitre is endemic, this condition is engrafted upon it" (Hamig).

4. That "the secretion of the gland in the diffuse parenchymatous hypertrophy is increased in quantity, and is altered in quality" (Hamig, Edwards).

Credit is due to the Berne Clinic for having shown us the proper plan of procedure. The low mortality is largely due to the excellent rules formulated by Kocher, the essence of which is not to attempt too much surgery on these cases at one time.

Very severe cases are subjected to pre-

liminary treatment, such as rest, the use of the ice-bag over the heart and goitre, until some improvement occurs. Then the ligation of a single artery, followed by intermission, and possibly further treatment, followed by the ligation of a second artery, and after another lapse, the removal of one lobe of the gland, thus graduating the surgery in harmony with the patient's condition. Especially is surgery indicated where the vascular symptoms predominate. During the operation the greatest care is observed in the hemostasis, since the blood of these patients is toxic in character and its absorption is always followed by an increase of the symptoms, and in some cases by the death of the patient. For the same reason drainage should be freely established, as the danger in these cases is usually during the first twenty-four hours after the operation, which represents the period during which the excess of secretion liberated during the operation is returned to the victim with possibly an overwhelming effect, as it has been said that the nearer to the normal we reduce the gland or its blood supply, the prompter will be the cure.

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The Lancet-Clinic

*A Weekly Journal of Medicine
and Surgery.*

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Published at 317 W. Seventh Street, Cincinnati.
Subscription: \$3.00 per annum.